UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/725,009	12/02/2003	Andrew Geall	1530.0620001/EKS/UWJ	3175

26111 7590 06/10/2008

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.
1100 NEW YORK AVENUE, N.W.
WASHINGTON, DC 20005

EXAMINER	
HINES, JANA A	

ART UNIT	PAPER NUMBER
1645	

MAIL DATE	DELIVERY MODE
06/10/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/725,009	GEALL, ANDREW	
	Examiner	Art Unit	
	JaNa Hines	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 March 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5-8,11 and 13-45* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1-3,5-8,11,13-22,29-37,40 and 43* is/are allowed.

6)☒ Claim(s) *23-28,38,39,41,42,44 and 45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/10/08*.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *3/5/08*.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Amendments

1. The amendments filed March 10, 2008 have been entered. Claims 1 and 29-36, have been amended. Claims 4, 9-10 and 12 are cancelled. Claims 1-3, 5-8, 11, and 13-45 are under consideration in this office action.

Withdrawal of Rejections and Objections

2. The following rejections have been withdrawn in view of applicants' amendments and arguments:

a) The new matter rejection of claims 1-3, 5-9, 11, and 13-45 under 35 U.S.C. 112, first paragraph;

b) The rejection of claims 1-2, 5-9, 11,13, 15-22, 29-32, 37, 40 and 43 under 35 U.S.C. 102(b) as being anticipated by Evans (WO 02/00844) and Volkin et al., (WO 97/408839) further in view of Hunter et al., (US Patent 5,811,088);

c) The rejection of claim 3 under 35 U.S.C. 103(a) as being unpatentable over Evans (WO 02/00844), Volkin et al., (WO 97/408839) and Hunter et al., (US Patent 5,811,088) further in view of Balasubramaniam (US Patent 5,824,322);

d) The rejection of claims 11 and 13-14 under 35 U.S.C. 103(a) as being unpatentable over Evans (WO 02/00844) Volkin et al., (WO 97/408839) and Hunter et al., (US Patent 5,811,088) further in view of Munsunuri et al., (WO 99/21591);

e) The rejection of claims 33-36 under 35 U.S.C. 103(a) as being unpatentable over Evans (WO 02/00844), Volkin et al., (WO 97/408839) and Hunter et al., (US Patent 5,811,088) further in view of Felgner et al., (US Patent 5,459,127); and

f) The objection of claims 25-26.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Claims 23-28, 38-39, 41-42 and 44-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Evans (WO 02/00844) in view of Volkin et al., (WO 97/408839).

Claims 23-24 are drawn to a product; Claims 25-26 are drawn to a stable, monodispersed product. Claims 27-28 are drawn to a product. Claims 38-39 are drawn to a stable, monodispersed product. Claims 41-42 are drawn to the produced product. Claims 44-45 are drawn a product.

Evans teach the preparation of compositions comprising a polynucleotide, nonionic block copolymers such as polyoxyethylene (POE)/polyoxypropylene (POP) and a cationic surfactant (POP) at a temperature below the cloud point of said block copolymer to form a mixture (page 3, lines 5-8 and 31-34 and page 32, lines 23-34).

Evans states that stabilized vaccines and alternative formulations, including lyophilized formulation have been taught by the incorporated WO 97/40839 reference (page 31, lines 15-18). Evans teaches the Preparation of CRL-1005 (block copolymer) formulations containing DNA and the cationic surfactant by mixing or vortexing the components at temperatures below the cloud point of the polymer, approximately 6-7°C (page 32, lines 23-34). Evans teaches mixing the components at temperatures below the cloud point. Evans recites the general POE/POP formula: $HO(C_2H_4O)_a(C_3H_60)_b(C_2H_40)_a$ H, wherein (b) represents a number such that the molecular weight of the hydrophobic POP portion (C_3H_60) is less than 20,000 daltons and wherein (a) represents a number such that the percentage of hydrophilic POE portion (C_2H_4O) is between approximately 1% and 40% by weight (page 4, lines 10-17). Evans discloses surface-active block copolymer represented by CRL-005 (page 13, lines 19-21).

Evan teaches polynucleotide formulations comprising a cationic surfactant along with the block copolymer (page 13, lines 22-26). Evan teaches the cationic surfactants not limited to: benzalkonium chloride (BAK), benzethonium chloride, cetramide (which contains tetradecyltrimethylammonium bromide, dedecyltrimethylammonium bromide hexadecyltrimethyl ammonium bromide, cetylpyridinium chloride and cetyl trimethylammonium chloride (page 13, lines 26-34). The composition comprises other excipients, such as glycerol (page 23, lines 10-14). Evans teaches the inclusion of glycerol, an amorphous cryoprotectant, as defined by the specification at paragraph [0079]. The vaccines include a saline solution such as phosphate buffered saline (PBS) (page 30, lines 18-20). The physiologically acceptable buffer in Figure 3 shows the use

of 10mM sodium phosphate buffer (page 13, lines 5-27). Thus Evan teaches sodium phosphate buffer within the range of about 5mM to about 25mM.

Evans teaches the concentration range of the respective polynucleotide be from about 0.5 mg/ml to about 7.5 mg/ml, the POE and POP block copolymer be at a concentration of from about 1 to about 70 mg/ml and that the cationic surfactant be at a concentration of 0.1 to 10mM (pages 21-22, lines 32-1). Therefore Evan discloses the concentrations of the cationic surfactant at about 0.1 to 5mM, the block copolymer at about 1 to about 50 mg/ml and the polynucleotide at about 1 mg/ml to about 50 mg/ml. Evans teaches the formulation was stored at –70C and then allowed to thaw to room temperature (page 33, lines 8-9). Evans teaches providing formulations that provide for long-term stability of the vaccines (page 30, lines 22-23). However Evans do not teach a product further comprising a monosaccharide, disaccharide or oligosaccharide compound.

Volkin et al., teach lyophilized DNA formulation comprising amorphous disaccharide sugars, explicitly sucrose and lactose greatly stabilize the DNA (page 81, lines 11-13). Figure 12 shows lyophilized DNA formulations containing lactose or sucrose and PBS (page 15, lines 27-30). The formulation also comprises 4-5% mannitol (page 15, lines 25-31). Volkin et al., teach preparations and compositions drawn to the compound being a monosaccharide, disaccharide or oligosaccharide and the produced products. Volkin et al., teach the inclusion of mannitol, a crystalline bulking agent, as defined by the specification at paragraph [0081]. Thus, Volkin et al., teach a mixture having 1% to 20% of a crystalline bulking agent. Volkin et al., teach lyophilization allows

for greater DNA stability and effectively stabilizes DNA vaccines (page 81, lines 7-11). Volkin et al., teach that during storage DNA vaccines undergo accelerated physiochemical changes, thus Volkin et al., teach formulations to optimize the stability of the DNA (page 9, lines 9-25). Volkin et al., also teach the lyophilization of DNA formulation enhances DNA stability, by reducing molecular motion, and formulations that provide the highest stability include buffers, glycerol and high DNA concentrations (page 11-12, lines 28-5).

It is noted that Since the Patent Office does not have the facilities for examining and comparing applicants' composition or product with the composition or product of the prior art reference, the burden is upon the applicants to show an unobvious distinction between the material structural and functional characteristics of the claimed products of the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594. It is further noted that "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of identification. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted). See also M.P.E.P 2113 [R-1] entitled Product-by-Process Claims: Product-By Process Claims Are Not Limited To The Manipulations Of The Recited Steps, Only The Structure Implied By The Steps. There

appears to be no structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art.

Therefore it would have been prima facie obvious at the time of applicants' invention to apply the lyophilized composition polynucleotide formulations comprising saccharide compounds and crystalline bulking agents as taught by Volkin et al., to Evans lyophilized composition comprising: a polyoxyethylene (POE) and polyoxypropylene (POP) block copolymer; (ii) a polynucleotide; (iii) a cationic surfactant; in order to optimize the stability of the polynucleotide and provide stable long term polynucleotide formulations in order to provide sterile block copolymer formulations. One of ordinary skill in the art would have a reasonable expectation of success by modifying the prepared product because both Evans and Volkin et al., teach the desirability of providing stable polynucleotide vaccines achieved by the specific formulations of Evans and Volkin et al., since Volkin et al., teach that disaccharide sugars such as sucrose and lactose greatly increase stabilization of lyophilized polynucleotide formulations. Moreover, one of ordinary skill in the art would have a reasonable expectation of success by modifying the lyophilized composition because both Evans and Volkin et al., teach the desirability of providing formulations containing block copolymers at a temperature at which they are soluble, i.e., below their cloud point. Finally it would have been prima facie obvious to combine the invention of Evans, and Volkin et al., to advantageously decreased physiochemical changes of the polynucleotides formulations during their storage and produce a stable, monodispersed

product produced by the cold filter method, since the prior art teaches that such techniques are well known to create sterile compositions.

Conclusion

4. Claims 1-3, 5-8, 11, 13-22, 29-37, 40 and 43 are drawn to allowable subject matter, since the prior art does not teach of suggest recited method of preparing a lyophilized composition as instantly claimed.

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 571-272-0859. The examiner can normally be reached Monday thru Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Shanon Foley, can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ja-Na Hines
December 4, 2007

/Mark Navarro/

Primary Examiner, Art Unit 1645